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PUBLIC HEALTH REPORTS

VOL. 35

JULY 9, 1920.

No. 28

UTILITY OF ANTIPLAGUE VACCINES AND SERUMS.

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Vaccine. Early in the modern studies of plague immunity an experimental foundation for antiplague vaccination was laid by the French (1) and German (2) workers. It may be noted, however, that immunity in animals, induced by vaccination with killed cultures, is not of a very high grade and is not readily induced, even under favorable conditions.

Vaccines.—Antiplague vaccine was first used on man in 1897 by Haffkine (3), who employed old killed broth cultures in what we would consider rather large doses. The excellent results reported by him in the way of protection against infection and in the reduction in the severity of attacks when complete immunity was not afforded, have become widely known. Briefly, Haffkine claimed a reduction of attacks among the vaccinated to one-fourth or less compared with those among the control (nonvaccinated) group and a very pronounced reduction in case fatality.

The much-quoted Byculla House of Correction experiment (4) covers an observation on rather small groups of vaccinated and of nonvaccinated persons, apparently comparable in every way, and seems to show that the vaccination gave protection, even as early as the day following the inoculation. This would presuppose a much earlier development of antibodies than seems possible from our present knowledge of active immunity. Cases continued to occur among members of the nonvaccinated group for eight days following vaccination, making a total of 12 attacks with 6 deaths from a group of 185 persons, while but two cases, both of which recovered, occurred among the 153 who were vaccinated.

A most puzzling feature in connection with some of Haffkine's later work on large groups of persons was the apparently very marked reduction in the general death rate among the vaccinated persons, even when the improvement which might be considered due to reduced plague mortality had been excluded. (5) This naturally threw some doubt on the validity of the numerical results in relation to plague.

In the hands of some other observers in India the results were by no means so brilliant as those reported by Haffkine, though the figures practically always pointed to a favorable influence of the prophylactic, as either the incidence or the case mortality, or both, were reduced.

The evidence was carefully examined by a commission appointed by the Government of India. A reading of the report of this commission will convince anyone that while the data were examined in a very critical manner, yet it was conceded that the evidence pointed decidedly to the value of vaccination. Anti plague vaccination is used in India at present to some extent.

Since Haffkine introduced his vaccine, some modifications have been made which do not require special discussion, though some special features developed in recent research demand consideration.

Rowland expresses the opinion that the uses of different strains (9) of the plague organism may have a bearing on the efficiency of the vaccine, and suggests that this may account for the failure of Haffkine's vaccine in the Dutch East Indies. In the light of this it would seem desirable to prepare a vaccine from a strain of the bacillus isolated in the locality where the prophylactic is to be employed. The same worker also presents experimental evidence that the growth in serum medium (10) of the organism used for the preparation of the vaccine produces a better immunizing agent than the broth growth of the same organism.

Sensitized vaccines have been employed, but there is no experimental evidence of their superiority and no record of any observations on large groups of men.

Strong (6), working in the Philippines, came to the conclusion that the inoculating of humans with living avirulent cultures of the plague bacillus afforded a promising method of prophylaxis, but this procedure has never been given a sufficiently extensive trial to demonstrate its value under other than laboratory conditions.

In concluding this brief review of vaccination in plague we must state that we are not acquainted with any evidence indicating that vaccination has ever controlled an outbreak.

Serums: Yersin (7 and 8) early prepared a serum by the immunization of horses with dead, and later with living, cultures in the usual manner for preparing antibacterial serums. This procedure was modified by Lustig and Galeotti (8), who used as an antigen for the immunization of horses a substance which they called "nucleo-albumin," obtained from the bacterial cells of the plague bacillus by a special process.

Rowland (11) also used a derivative of plague bacilli for the immunization of horses for the production of a therapeutic serum and

found that it had antitoxic and protective properties and was definitely curative in infected rats.

Antiplague serum, particularly the one made according to Yersin's method, has been used both as a prophylactic and in the treatment of those sick of plague.

Dealing first with the prophylactic use of serum, it may be stated that evidence for or against its value is meager, as no observations are on record in which its use has been extensive and adequately controlled. It is certain that no complete or durable immunity is produced; indeed, it has been stated that whatever protection is conferred does not extend beyond 10 days. We could scarcely hope for a very long passive immunity even from a highly potent serum, and, in comparison with some others, antiplague serum can not be considered as especially potent. When we consider the unpleasant consequences that occasionally follow the injection of horse serum, it appears that the use of antiplague serum as a prophylactic need not be seriously considered until we have a more potent preparation or possess clearer evidence of the value of the serum now in use than is available at present.

The therapeutic use of serum has been tested in many well-controlled series of cases, usually with some apparent advantage on the side of the serum-treated cases, though the reduction of mortality has never been very conspicuous, and indeed in some series there was no observable influence of the serum.

It is obvious that the quality of the serum and the dose in which it is employed may be factors that are of the greatest importance. There is a report by Seeman (12) of the use of the serum in the New Orleans outbreak of 1914 in which brilliant results appear to have been secured by large doses of the serum. As much as 200 cc. was given at a dose and the large doses were repeated. This stands as an almost isolated example of an experience in which definite benefit appears to have been derived from the preparation.

It seems rather unfortunate to those who are called on for advice in connection with a plague outbreak to find that popular and professional interest is so frequently centered on the subject of prophylaxis by vaccines or serums and on treatment by serum when, in fact, the situation demands active measures against rodents. Under American conditions at least it is not a matter of much importance whether biological products are used in a prophylactic way or not. The health officer need give but little consideration to them in his plans to deal with an outbreak of bubonic plague. If people want to be vaccinated for prophylactic purposes there is no objection to complying, but the community should not be allowed to delude itself into the belief that plague may be controlled in this manner. The essential features of an antiplague campaign should be the ex-

termination of rodents and not immunization by means of vaccines or serums.

1. Yersin, Calmette and Borrel: *Ann. de l'Inst. Pasteur* 1895, 9, p. 589.
2. Bericht der deutschen Pestcommission. *Arb. a. d. Kais. Ges.-Amt*, Vol. 18, 1899.
3. Report of Indian Plague Commission. Vol. V, 1901.
4. Same, p. 196.
5. Same, p. 209.
6. *Philippine Journal of Science*, Sec. B. Vol. 2, 1907, p. 238.
7. Yersin, *Ann. de l'Inst. Pasteur*. Vol. 11, 1897.
8. Referred to by Kolle and Wassermann. *Handbuch der pathogenen Mikroorganismen*, 1904; 4th Vol. Second part, p. 949.
9. *Journal of Hygiene*, Plague Supplement, No. IV, p. 759, 1915.
10. *Journal of Hygiene*, Plague Supplement, No. III, p. 440, 1914.
11. *Journal of Hygiene*, Plague Supplement, No. I, p. 20, 1912.
12. *American Journal of Tropical Diseases*, Vol. III, p. 281, 1915.

PELLAGRA INCIDENCE IN RELATION TO SEX, AGE, SEASON, OCCUPATION, AND "DISABLING SICKNESS" IN SEVEN COTTON-MILL VILLAGES OF SOUTH CAROLINA DURING 1916.¹

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Introduction.

In the spring of 1916 we began a study of pellagra in certain cotton-mill villages of South Carolina. The results of that portion of the first year's study dealing with the relation of diet to pellagra incidence have already been reported.² In the present paper we desire to report the results of the part of the study dealing with the incidence of the disease in relation to certain social factors. Although a number of students have made somewhat similar studies, which we hope to review in a later paper, this, so far as we are aware, is the first time that the actual age and sex incidence of the disease have been determined for a population enumerated in direct connection with the study.

Locality and Population.

The study was made in seven representative cotton-mill villages situated in the northwestern part of South Carolina. The population of each was composed almost entirely of mill employees and their families. The few Negro families present and living in a quarter somewhat apart were not considered, so that our study deals with an exclusively white population which, with hardly a single exception, was of Anglo-Saxon stock, born in this country of American-born parents. We also excluded from our study

¹ From Field Investigations of Pellagra. Manuscript submitted for publication Feb. 5, 1920. Goldberger, Wheeler, and Sydenstricker, 1920.